

### **REMARKS**

Claims 1-23 are pending in the application. Claims 1-10 are withdrawn from consideration as being drawn to a non-elected invention and claims 11-23 are under examination. Claims 11-23 are rejected under 35 U.S.C. § 112, first and second paragraphs, and claims 11-19 are rejected under 35 U.S.C. § 103(a). In addition, the specification should be amended to recite the priority claim and to more clearly indicate trademarks.

#### **Substitute Specification**

The specification has been amended to recite the priority claim, to place trademark names in all-capital letters, and to provide generic terminology for trademarks. Applicants submit herewith a clean copy of the substitute specification and a marked-up copy of the specification. Applicants believe that no new matter is added by the amendments to the specification.

#### **Priority Claim**

The Office Action states that the first paragraph of the specification should be amended to recite the instant application's priority claims to PCT/US00/25166 and 60/153,698. In response, Applicants have amended the specification by inserting a priority claim and submit herewith a substitute specification as stated above.

#### **Information Disclosure Statement**

The Office Action states that the Information Disclosure Statement (IDS) filed August 13, 2002 fails to comply with the provisions of 37 C.F.R. §§ 1.97 and 1.98 and MPEP § 609 because a copy of reference 1 on page 1 of 7 was not included among the papers filed with the instant application. Thus, the reference has been lined through and the information referred to therein was not considered as to the merits.

In response, Applicants respectfully point out that the above-referenced IDS complies with 37 C.F.R. §§ 1.97 and 1.98 and MPEP § 609; thus, Applicants believe that the Office's failure to consider the cited reference was in error. The reference lined

through and not considered by the Office is U.S. Patent No. 6,080,728, issued to James A. Mixson on 06/27/2000. Specifically, MPEP § 609.04(a)(II), citing 37 C.F.R. § 1.98(a)(2)(ii), states that the requirement for a copy of each U.S. patent listed in a IDS *has been eliminated*, unless required by the Office. In view of the foregoing, Applicants had no prior notice that they would be required to submit a copy of an issued U.S. patent. Thus, it is improper for the Office to penalize Applicants for not submitting a copy. For the Examiner's convenience, a copy of U.S. Patent No. 6,080,728 is included herewith.

In view of the fact that the IDS filed August 13, 2002 is in compliance with the provisions of 37 C.F.R. §§ 1.97 and 1.98 and MPEP § 609, Applicants respectfully request that the Examiner consider U.S. Patent No. 6,080,728 and provide notice of such consideration of the reference to Applicants.

#### Use of Trademarks in Specification

The Office Action states that the use of trademarks such as Endostatin<sup>TM</sup>, Streamline<sup>TM</sup>, Sepharose<sup>TM</sup>, and Toyopearl<sup>TM</sup> in the specification should be capitalized wherever they appear and be accompanied by the generic terminology.

In response, Applicants have amended the specification to capitalize Streamline<sup>TM</sup>, Sepharose<sup>TM</sup>, and Toyopearl<sup>TM</sup> and to provide generic terminology. Applicants note that the term "endostatin" has been in generic use as of the priority date of the instant application (see, e.g., O'Reilly et al. "Endostatin: An Endogenous Inhibitor of Angiogenesis and Tumor Growth," *Cell* 88:277-285 (1997); submitted herewith). Thus, to avoid confusion to the public, Applicants have amended the specification to replace the term "Endostatin<sup>TM</sup>" with "endostatin." Applicants submit herewith a clean copy of the specification and a marked-up copy of the specification to indicate where changes have been made. Applicants believe that no new matter is added by these amendments.

Rejections under 35 U.S.C. § 112, Second Paragraph

*A. Recitation of Trademarks in Claims*

Claims 11-23 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness, because claims 11, 15, 16, 18, 20, and 22 contain the trademark/tradename Endostatin<sup>TM</sup>.

As stated above, Applicants have amended the claims to replace “Endostatin<sup>TM</sup>” with “endostatin.” The term “endostatin” has been in generic use as of the priority date of the instant application. Furthermore, the instant specification describes the physical characteristics of endostatin (e.g., size and amino acid sequence; see, e.g., page 9, line 21, through page 10, line 11, and page 29, line 1, through page 33, line 10, of the specification as originally filed). Thus, as amended, claims 11-23 clearly identify and describe endostatin and Applicants request that this aspect of the rejection be withdrawn.

*B. Essential Elements*

Independent claim 11 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting essential elements.

In response, Applicants have amended claim 11 to specifically recite the source of endostatin applied to each column and to clarify that “a first cation exchange column and expanded bed chromatography” constitutes two method steps. In view of the foregoing amendments, Applicants request that this aspect of the rejection be withdrawn.

*C. Lyophilizing and Reconstituting Endostatin*

Claims 16, 21, 22, and 23 are rejected for recitation of steps comprising lyophilizing endostatin and reconstituting lyophilized endostatin. The Office Action states that because lyophilization and reconstitution do not constitute a purification method it is unclear how these claims further limit the method of claim 11.

Applicants respectfully point out that lyophilization and reconstitution are steps that are commonly employed at the end of protein purification methods. Recitation of an additional step in a process further limits the process. Thus, Applicants request that this aspect of the rejection be withdrawn.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 11-23 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement.

Applicants have amended independent claim 11 to recite elution buffers comprising specific components. Support for the amendments is found, e.g., at page 36, line 6, through page 40, line 21 of the specification as originally filed. No new matter was added by this amendment. In view of the foregoing amendment Applicants request that the rejection be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 11-13, 15, 16, and 18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dhanabal in view of Johansson and further in view of Goldstein (the '295 patent).

Dhanabal teaches expression of recombinant mouse endostatin in *Pichia Pastoris*. Johansson teaches a method of large scale recovery and purification of recombinantly produced protein by expanded bed cation exchange chromatography, phenyl sepharose fast flow chromatography, and anion exchange chromatography. The '295 patent teaches purification of proteins by anion or cation exchange chromatography, hydrophobic interaction chromatography, concentration by diafiltration, and subsequent lyophilization.

Claim 14 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Dhanabal in view of Johansson and the '295 patent as applied above to claim 11 in view of Hjorth. Horth reviews expanded bed chromatography, including STREAMLINE™ SP resin.

Claim 17 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Dhanabal in view of Johansson and the '295 patent as applied above in view of Davis (the '811 patent). The '811 patent teaches polyethesulfone membranes.

Claim 19 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Dhanabal in view of Johansson and the '295 patent as applied above in view of Chang

(the '865 patent). Change teaches that 0.1 M citrate-phosphate buffer is a suitable elution buffer for eluting IFN-gamma.

As discussed above with regard to the rejection under § 112, first paragraph, independent claim 11 is amended herein to recite specific elution buffer components. The remaining claims depend, directly or indirectly, from claim 11. The cited references, alone or in combination, do not teach or suggest the specific elution buffer components and concentrations thereof as currently recited by the claims. Thus, these references do not render obvious the claims as amended and Applicants request that the § 103(a) rejection be withdrawn.

**CONCLUSIONS**

Applicants believe that this response is fully responsive to the present Office Action. Accordingly, Applicants submit that the application is in condition for allowance and such action is respectfully requested.

Submitted herewith is a request for extension of time under 37 C.F.R. § 1.136(a) to extend the period for response by three months to April 10, 2008. Also submitted herewith is payment of the required fee under 37 C.F.R. § 1.17(a)(3) for the three-month extension of time. No additional fees are believed due. However, the Commissioner is hereby authorized to charge any additional fee that may be required or to credit any overpayment to Deposit Account No. 11-0855.

If the Examiner believes that informalities remain in the application that can be corrected by Examiner's amendment or there are other issues that can be resolved by a telephone interview, a telephone call to the undersigned at (404) 815-6139 is respectfully solicited.

Respectfully submitted,  
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